

UNITED STATES PATENT AND TRADEMARK OFFICE  
**CERTIFICATE OF CORRECTION**

PATENT NO. : 7,022,893 B1  
APPLICATION NO. : 09/581528  
DATED : April 4, 2006  
INVENTOR(S) : M. Takeda et al.

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It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the title of the printed patent, item (56), References Cited, "6,395,960" should be --6,395,690--.

At column 35, line 26 (claim 1, line 1) of the printed patent, "having" should be --whose genome comprises--.

At column 35, line 27 (claim 1, line 2) of the printed patent, after "wherein" insert --expression of--.

At column 35, line 28 (claim 1, line 3) of the printed patent, "overexpression" should be --accumulation--.

At column 35, line 31 (claim 2, line 2) of the printed patent, "animal" should be --mouse--.

At column 35, line 32 (claim 2, line 3) of the printed patent, after "DNA" delete "having a".

At column 35, line 36 (claim 3, line 1) of the printed patent, after "The" delete "non human".

At column 35, line 37 (claim 3, line 2) of the printed patent, "has" should be --genome comprises--.

At column 35, line 38 (claim 3, line 3) of the printed patent, after "encoding" delete "around".

At column 35, lines 39-40 (claim 3, lines 4-5) of the printed patent, "in an amino acid sequence of the presenilin-1 protein" should be --of a mouse presenilin-1 protein as set forth in SEQ ID NO: 3--.

At column 35, line 42 (claim 3, line 6) of the printed patent, "5'-TGTGGTCGGGATGATYGCC AVC CACTGGAAAGGCC-3' (SEQ ID NO: 18)" should be --5'-TGTGGTCG GGATGATYGCC AVC CACTGGAAAGGCC-3' (SEQ ID NO: 18)--.

At column 35, line 45 (claim 3, line 9) of the printed patent, "the underlined bases" should be --wherein AVC--.

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It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

At column 35, line 47 (claim 4, line 1) of the printed patent, after "The" delete "non human".

At column 35, line 48 (claim 4, line 2) of the printed patent, "has" should be --genome comprises--.

At column 35, line 49 (claim 4, line 3) of the printed patent, after "encoding" delete "around".

At column 35, lines 50-51 (claim 4, lines 4-5) of the printed patent, "in an amino acid sequence of the presenilin-1 protein" should be --of a mouse presenilin-1 protein as set forth in SEQ ID NO: 3--.

At column 35, line 52 (claim 4, line 6) of the printed patent, "5'-TGTGGTCGGGATGATMGCC ACC CACTGGAAAGGCCC-3' (SEQ ID NO: 19)" should be --5'-TGTGGTCGGGATGATYGCC ACC CACTGGAAAGGCCC-3' (SEQ ID NO: 19)--.

At column 35, line 54 (claim 4, line 8) of the printed patent, "the underlined bases" should be --wherein ACC--.

At column 35, line 57 (claim 5, line 2) of the printed patent, "has" should be --genome comprises--.

At column 35, line 58 (claim 5, line 3) of the printed patent, after "encoding" delete "around".

At column 36, lines 58-59 (claim 5, lines 3-4) of the printed patent, "in an amino acid sequence of the presenilin-1 protein" should be --of a mouse presenilin-1 protein as set forth in SEQ ID NO: 3--.

At column 35, line 62 (claim 5, line 6) of the printed patent, "5'-TGTGGTCGGGATGATYGCC NNN CACTGGAAAGGCCC-3' (SEQ ID NO: 20)" should be --5'-TGTGGTCGGGATGATYGCC NNN CACTGGAAAGGCCC-3' (SEQ ID NO: 20)--.

At column 35, line 67 (claim 5, line 11) of the printed patent, "the underlined bases" should be --wherein NNN--.

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At column 36, line 25 (claim 6, line 1) of the printed patent, after "The" delete "non human".

At column 36, line 26 (claim 6, line 2) of the printed patent, after "transferred" insert --into a mouse ES cell genome--.

At column 36, line 28 (claim 7, line 1) of the printed patent, "having" should be --whose genome comprises--.

At column 36, line 29 (claim 7, line 2) of the printed patent, after "DNA" delete "having a".

At column 36, line 33 (claim 7, line 6) of the printed patent, after "wherein" insert --expression of--.

At column 36, line 34 (claim 7, line 7) of the printed patent, "overexpression" should be --accumulation--.

At column 36, line 37 (claim 8, line 1) of the printed patent, "having" should be --whose genome comprises--.

At column 36, line 38 (claim 8, line 2) of the printed patent, after "DNA" delete "having".

At column 36, line 42 (claim 8, line 6) of the printed patent, after "wherein" add --expression of--.

At column 36, lines 42-43 (claim 8, lines 6-7) of the printed patent, "overexpression" should be --accumulation--.

At column 36, line 45 (claim 9, line 1) of the printed patent, "having" should be --whose genome comprises--.

At column 36, line 46 (claim 9, line 2) of the printed patent, "the" should be --an--.

At column 36, line 47 (claim 9, line 3) of the printed patent, after "wherein" add --expression of--.

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At column 36, lines 47-48 (claim 9, lines 3-4) of the printed patent, "overexpression" should be --accumulation--.

At column 36, line 53 (claim 10, line 4) of the printed patent, after "mouse" add --whose genome comprises a mutant presenilin-1 gene--.

At column 36, line 59 (claim 10, line 10) of the printed patent, after "mouse" add --whose genome comprises a mutant presenilin-1 gene--.

At column 37, line 4 (claim 12, line 2) of the printed patent, after "cell" add --comprising a mutant presenilin-1 gene--.

At column 37, line 4 (claim 12, line 2) of the printed patent, after "mouse" add --whose genome comprises a mutant presenilin-1 gene--.

At column 37, line 5 (claim 12, line 3) of the printed patent, after "culture" add --, wherein expression of the mutant presenilin-1 gene results in accumulation of Amyloid  $\beta$  42 in said culture--.

At column 37, line 8 (claim 13, line 3) of the printed patent, delete "the step of".

At column 37, line 8, (claim 13, line 3) of the printed patent, after "culture" add --comprising a mutant presenilin-1 gene--.

At column 37, line 9 (claim 13, line 4) of the printed patent, after "cell" add --comprising a mutant presenilin-1 gene--.

At column 37, line 10 (claim 13, line 5) of the printed patent, after "subcultured cell" add --; and determining effect of said test compound on Amyloid  $\beta$  42 formation in the cell culture or the subcultured cell--.

At column 37, line 11 (claim 14, line 1) of the printed patent, after "An" add --isolated mouse--.

At column 37, line 11 (claim 14, line 1) of the printed patent, "introduced with a plasmid comprising" should be --whose genome comprises--.

At column 37, line 12 (claim 14, line 2) of the printed patent, after "DNA" add --sequence--.

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It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

At column 37, line 16 (claim 15, line 1) of the printed patent, after "an" add --isolated mouse--.

At column 37, line 16 (claim 15, line 1) of the printed patent, after "embryo" add --of claim 14--.

At column 37, lines 16-17 (claim 15, lines 1-2) of the printed patent, "homologous recombination using the plasmid according to claim 1." should be --insertion of a mouse ES cell comprising a DNA sequence represented by the nucleotide sequence: 5'-TGTGGTCGGGATGATYGCCACCCACTGGAAAGGCC-3' (SEQ ID NO: 19) wherein Y represents T or C--.

At column 38, line 1 (claim 16, line 1) of the printed patent, after "gene-mutated" add --presenilin-1--.

At column 38, line 2 (claim 16, line 2) of the printed patent, delete lines 2-9 in its entirety and add --comprising introducing a DNA sequence encoding a presenilin-1 mutation into mouse ES cells, permitting the DNA sequence to undergo homologous recombination with the genome of said ES cell, thereby inserting the presenilin-1 mutation into the endogenous presenilin-1 gene, transferring said ES cell comprising the mutant presenilin-1 into a mouse embryo, transferring the embryo to a female mouse and developing the mouse to term--.

Signed and Sealed this

Sixteenth Day of October, 2007



JON W. DUDAS  
*Director of the United States Patent and Trademark Office*